



## APPENDIX II

### AMENDED SPECIFICATION PARAGRAPHS WITH AMENDMENTS INDICATED THEREIN BY BRACKETS AND UNDERLINING

Pages 1 and 2, replace the paragraph bridging these pages with the following:

The heretofore existing possibilities of administration (oral, parenteral) employing these substances are [dissatisfactory] unsatisfactory. There is a danger of acid-catalyzed chemical changes taking place in the stomach. In addition, these administration forms result in high variations in the plasma level, which are observed in particular, in the case of parenteral application (injection). Due to the plasma concentrations obtained either falling short of or exceeding the therapeutically desired plasma concentrations, habit-forming effects occur.

Page 5, fifth full paragraph, is amended as indicated below:

The substance according to the invention substantially consists of an acid-addition salt of a morphine alkaloid of the aforementioned formula I and a further organic acid. The term "substantially consisting of" signifies that impurities are contained only to an extent which is common. The substance [respectively] or the composition according to the present invention can be prepared and purified employing methods commonly used in preparative organic chemistry, so that the purified substance can

also be provided in p.A. or p.p.A. purity. The acid is, in particular, pharmaceutically acceptable. It, too, can be produced by means common methods if it is not yet available on the market.

Page 11, first full paragraph, is amended as indicated below:

Especially preferred penetration enhancers are polyoxethylene sorbitane fatty acids, such as Tween 20, or polyoxyethylene alcohols, such as, for example, [polymerisation] polymerization products of up to 10 molecules ethylene oxide, each with one molecule octanol, decanol or dodecanol, or mixtures of these [polimerization] polymerization products.

Page 13, first full paragraph, is amended as indicated below:

What kind of common additives are employed depends on the polymer used[:]. According to their function, they can be [divided] characterized, for example, [in] as tackifying agents, stabilizers, carriers and fillers. Physiologically acceptable substances suitable for this purpose are known to the man skilled in the art.

Page 14, first full paragraph, is amended as indicated below:

Such additives are, for example, polyacrylic acid carboxymethylcellulose and other [derivated polysaccharides] polysaccharide derivatives, especially acetyl starch or hydroxyethyl starch or combinations thereof.

Page 15,        third full paragraph, is amended as indicated below:

1 g (3.5 mMol) water-free morphine base were dissolved, while heating, in 100 ml methanol. Once the base had been completely dissolved in methanol, a solution of 756 mg (3.5 mMol) monomethylsebacic acid in 20 ml methanol was added. The combined solutions were [narrowed down] concentrated in the rotary evaporizer. After ca. 48 h at 5 °C the morphine monomethyl sebacate had crystallized. Solvent residues were removed using a vacuum pump. The crystals had a melting point of 146 °C.